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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/561,324

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06/10/2009

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EXAMINER

VIVLEMORE, TRACY ANN

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

06/10/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/561,324	Applicant(s) KRAYNACK ET AL.	
	Examiner Tracy Vivlemore	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-7,9,14,20-22,26-30,39-44,49,50 and 53-56 is/are pending in the application.
- 4a) Of the above claim(s) 53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-7,9,14,20-22,26-30,39-44,49,50,54 and 55 is/are rejected.
- 7) ☒ Claim(s) 56 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
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| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/11/08 and 3/9/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Election/Restrictions

Claim 53 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 6, 2008.

Claims 1-3, 5-7, 9, 14, 20-22, 26, 30, 39-44, 49, 50 and 54-56 are pending and examined on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5-7, 9, 14, 20-22, 26, 30, 39-44, 49, 50, 54 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fosnaugh et al. (US 2003/0143732, of record).

The claims are directed to compositions of first and second complementary oligomeric compounds wherein one strand is capable of hybridizing to a selected target

nucleic acid and wherein one strand comprises 2' modified nucleotides having 3'-endo conformational geometry at each position and one of the positions comprises a 2'-fluoro purine nucleotide. Specific embodiments recite which strand comprises the nucleotides having endo conformation, the presence of a stabilizing group such as a dTdT overhang, a 5'-phosphate, a capping moiety such as an inverted deoxy abasic moiety, that both strands have 3'-endo geometry, the identity of the modified nucleotide, the length of the oligomer, and the specific number and identity of the modified nucleotides.

Fosnaugh et al. disclose that short interfering RNAs, duplexes of 21-23 nucleotides that mediate RNA interference, comprise an antisense sequence complementary to a target gene and a sense sequence complementary to the antisense sequence. These siRNAs are useful for a variety of therapeutic, diagnostic, agricultural, target validation, genomic discovery, genetic engineering and pharmacogenomic applications. Chemically-modified siRNAs are expected to improve various properties of siRNAs including increased *in vivo* nuclease resistance and/or improved cellular uptake. Specific embodiments of siRNAs and chemically modified siRNAs are disclosed at pages 3-10. At paragraph 50 Fosnaugh et al. teach that siRNAs can comprise 2'-O-methyl and/or 2'-deoxy-2'-fluoro modifications in the sense strand and the antisense strand and that siRNAs optionally can further comprise a terminal cap molecule at the 3', 5', or both 3' and 5'-ends of the sense or antisense strands. Fosnaugh et al. teach at paragraph 65 that capping moieties include deoxy abasic residues. At paragraph 46 Fosnaugh et al. teach that siRNAs can comprise a 5' phosphate group and at paragraph 68 teach that siRNAs can comprise conjugate

groups. Fosnaugh et al. teach siRNAs having dTdT overhangs in figure 4 (described at paragraph 145)

While Fosnaugh et al. do not explicitly teach substitution of each of the nucleotides other than 2'-OH as 3'-endo nucleotides or the particular number of 2'-F and 2'-OMe substitutions recited in the claims, it would be obvious to one of ordinary skill in the art to make siRNAs comprising chemical modifications and because Fosnaugh et al. teach modified siRNAs comprising both 2'-F and 2'-OMe modifications in either the sense or antisense strands without regard to sequence or type of nucleobase and teach that such modifications are desirable to provide increased uptake and nuclease resistance, one of ordinary skill would find it a matter of routine optimization and design choice to predictably produce a siRNA where all positions contain a modification that provides 3' endo conformation. One of ordinary skill in the art would further recognize based on the teachings of Fosnaugh et al. of 5' phosphates, terminal caps, conjugates and overhangs of dTdT nucleotide that inclusion of such moieties is further a matter of design choice in order to provide a siRNA that has the best combination of properties for a particular application.

Response to Arguments

Upon further consideration, the rejection of record is withdrawn with regard to the specific pattern of modifications recited in claim 56.

Applicants traverse the rejection of record by arguing the Fosnaugh application fails to teach or suggest oligomeric compounds of the claims, arguing that the Fosnaugh

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application provides generalized teachings regarding chemical modification of RNA, reciting a broad list of possible chemical modifications for oligomeric compounds but does not describe compounds in which each nucleoside bears a chemical modification and has 3'-endo conformational geometry. Applicants conclude that based on this limited guidance one of ordinary skill would have had no reason to design and produce such compounds.

This argument is not persuasive because while Fosnaugh may not exemplify an siRNA wherein every position contains a modified sugar, Fosnaugh teaches the inclusion of modified sugars such as 2'-F and 2'-OMe in a permissive manner, teaching that the strands may contain 10 or more modifications, which the person of ordinary skill would recognize embraces modification at every position within a strand.

Allowable Subject Matter

Claim 56 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is (571)272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service

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center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Primary Examiner
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